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Filed : March 15, 2001

REMARKS

This amendment addresses the Official Action mailed March 9, 2005 (Applicant had already filed an Amendment along with an RCE on June 8, 2005). This amendment also addresses the substance of a personal interview on September 22, 2005. In view of the discussions with Examiner, Applicant has now canceled all pending claims and presents for examination new Claims 60-85. The Notice of Non-Compliant Amendment mailed August 23, 2005 is therefore deemed moot.

Written Description Support

During the interview, the Examiner indicated that she was concerned about written description support for the amendments discussed. For the most part, the new claims find literal support in the claims as originally filed.

More particularly, the specification provides explicit written description support for a vaccination method comprising a step of introducing into the mammal by disrupting the stratum corneum an effective dose of the target antigen or an epitope(s) thereof. See e.g., page 10, line 28 to page 11, line 7, which describes various non-topical means for “introducing into” a mammal, including “injection or mechanical or chemical disruption of the stratum corneum...”. Furthermore, such methods of introducing antigen “into” the mammal by disrupting the stratum corneum are distinguished from topical methods of applying antigen “onto” the stratum corneum. In addition, on page 23, lines 22-29, the specification sets forth a paragraph under the heading “Intradermal Delivery”, which provides that “the stratum corneum can be penetrated using sharp instruments....” This paragraph goes on to describe injections using traditional beveled needles, introduction of antigens using pronged instruments (e.g., tine test), high pressure, needle-free injection systems, etc. In addition, on page 39, lines 13-23, the specification states that the invention is “useful for antigen(s) delivered to the host by any means. The antigen could be delivered by penetration of the stratum corneum with needles (as shown in Figures 10-12) or by other commonly used invasive procedures... Alternatively, dendritic cells could be exposed to the antigen(s) by... disruption of the stratum corneum using abrasion, chemical peels, lasers or other physical or chemical means...” Thus, Applicant respectfully asserts that the specification provides ample descriptive support for a step of introducing antigen into the mammal by disrupting the stratum corneum.

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Support for a step of administering to the mammal a topical treatment which in the absence of any antigen is sufficient to increase the number of dendritic cells migrating to a lymphoid organ can be found throughout the specification. See e.g., page 31, line 37, stating that “[t]he frequency of dendritic cells in the inguinal lymph nodes of untreated C57BL/6 mice... is 4,636 (SD 1,796) dendritic cells per node. The results shown in Figure 9A provide dramatic evidence that this topical method to induce dendritic cell migration/maturation [dibutyl phthalate and acetone] causes large numbers of dendritic cells (~60,000) to enter the draining lymph node, even *in the absence of any antigen*. Further, Applicant describes potential clinical benefits of inducing dendritic cell migration/maturation in the absence of antigen. See e.g., page 28, line 1: “[i]n some instances, it may be advantageous, merely to enhance Langerhans cell (immature dendritic cell) migration, without specifically administering any antigen. For example, where an individual has a skin cancer, such as melanoma or basal cell carcinoma, it may be useful in enhancing an immune response against the tumor to administer an inducer of Langerhans cell migration to sites surrounding the tumor...”. The specification provides numerous examples of ‘topical treatments’ including the genus of lipophilic molecules disclosed throughout the specification (see e.g., page 25, and original Claim 3). A variety of specific compounds are set forth on page 26, including dibutyl phthalate and camphor. Applicant also described the use of ultrasound as a topical treatment capable of increasing dendritic cell migration to the draining lymph node (see e.g., Fig. 9A and accompanying discussion). Accordingly, Applicant has both literal written support as well as empirical support for the step of administering a topical treatment, such as a lipophilic molecule or ultrasound, which in the absence of any antigen is sufficient to increase the number of dendritic cells migrating to a lymphoid organ.

Rejection under 35 U.S.C. §112

In the Office Action dated March 9, 2005, the Examiner maintained rejection of Claim 30 under 35 U.S.C. §112, first paragraph, for lacking written description. More specifically, the Examiner indicated that Claim 30 was rejected because the specification does not describe the structure of the endogenous inducer of dendritic cell migration and maturation. Claim 30 has been canceled without prejudice to pursue the subject matter in a later application. The new Claims do not recite any limitations related to the endogenous inducers. Accordingly, this

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rejection is deemed to be moot and Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §102

In the Office Action dated March 9, 2005, the Examiner maintained rejection of Claims 1,6,8,11,13,14,16 and 28-31 under 35 U.S.C. §102(b) as being anticipated by Dearman et al. These claims have been canceled and are replaced by new Claims 60-85. Accordingly, the present rejection is moot. Each of new Claims 60-85 recite *inter alia*, a vaccination method, comprising introducing into the mammal by disrupting the stratum corneum an effective dose of the target antigen or an epitope(s) thereof. Support for this limitation is detailed above (Written Description Support).

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed.Cir. 1986). “[A]nticipation requires that all of the elements and limitations of the claim are found within a single prior art reference.” *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991).

Applicant respectfully points out that Dearman fails to teach a vaccination method comprising a step of introducing into the mammal by disrupting the stratum corneum an effective dose of the target antigen or an epitope(s) thereof. Moreover, disruption of the stratum corneum is not an inherent feature of Dearman, which teaches only introducing FITC + dibutyl phthalate by topical route (i.e., by permeation through the intact stratum corneum). Thus, because each of new Claims 60-85 recites a step of introducing the target antigen into the mammal by disrupting the stratum corneum, Applicant respectfully asserts that Dearman cannot anticipate any of new Claims 60-85.

Rejections under 35 U.S.C. §103

Dearman in view of Mitragotri and Paul – In the Office Action dated March 9, 2005, the Examiner maintained rejection of Claims 1,6,8,11,13,14,16,17,21,22,27-31 and 51 under 35 U.S.C. §103(a) as being obvious over Dearman in view of Mitragotri (WO 97/04832) and Paul (Vaccine research, 1995, Vol. 4, pp. 145-164). These claims have been canceled and replaced by new Claims 60-85. Accordingly, the present rejection is moot. Each of new Claims 60-85 recite

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inter alia, a vaccination method, comprising introducing into the mammal by disrupting the stratum corneum an effective dose of the target antigen or an epitope(s) thereof. Support for this limitation is detailed above (under Written Description Support).

Under MPEP §2143 “[t]o establish a *prima facie* case of obviousness... there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all/the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure...”

As detailed above, Dearman fails to teach introducing antigen into the mammal by disrupting the stratum corneum. Mitragotri teaches introducing antigen into the mammal by non-disrupting application of ultrasound to the intact skin. Paul teaches introducing antigen into the mammal by non-disrupting topical delivery across the intact skin using submicroscopic transfersome vesicles. Thus, the combination fails to teach a vaccination method, comprising *inter alia* introducing into the mammal by disrupting the stratum corneum an effective dose of the target antigen or an epitope(s) thereof as recited in all of new Claims 60-85. Accordingly, Applicant respectfully asserts that Dearman in view of Mitragotri and Paul cannot render obvious any of new Claims 60-85.

Dearman in view of King – In the Office Action dated March 9, 2005, the Examiner maintained rejection of Claims 1 18 and 24 under 35 U.S.C. §103(a) as being obvious over Dearman in view of King et al. (Vaccine, 1987, Vol. 5, pp. 234-238). These claims have been canceled and replaced by new Claims 60-85. Accordingly, the present rejection is moot. Each of new Claims 60-85 recite *inter alia*, a vaccination method, comprising introducing into the mammal by disrupting the stratum corneum an effective dose of the target antigen or an epitope(s) thereof.

As detailed above, Dearman fails to teach introducing antigen into the mammal by disrupting the stratum corneum. King teaches introducing antigen via the nasal mucosa, a method that avoids disrupting the stratum corneum. Thus, the combination fails to teach a

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vaccination method, comprising *inter alia* introducing into the mammal by disrupting the stratum corneum an effective dose of the target antigen or an epitope(s) thereof as recited in all of new Claims 60-85. Accordingly, Applicant respectfully asserts that Dearman in view of King cannot render obvious any of new Claims 60-85.

Dearman in view of Salyers – In the Office Action dated March 9, 2005, the Examiner maintained rejection of Claims 19 and 23 under 35 U.S.C. §103(a) as being obvious over Dearman in view of Salyers et al. (Bacterial Pathogenesis, 1994, pp. 8-14 and 144-145). These claims were directed to methods involving either introducing antigen via ingestion (Claim 19) or via delivery to respiratory, urogenital or gastrointestinal tracts (Claim 23); Claims 19 and 23 have been canceled without prejudice. None of new Claims 60-85 recite vaccination methods comprising introducing antigen by ingestion or via delivery to respiratory, urogenital or gastrointestinal tracts. Accordingly, the rejection is moot and does not apply to any of new Claims 60-85.

Dearman in view of Glenn – In the Office Action dated March 9, 2005, the Examiner maintained rejection of Claims 1, 6, 8, 11, 13-16, 27-31, 52, 53, 55, and 58 under 35 U.S.C. §103(a) as being obvious over Dearman in view of Glenn et al. (US 5,980,898). These claims have been canceled and replaced by new Claims 60-85. Accordingly, the present rejection is moot. Each of new Claims 60-85 recite *inter alia*, a vaccination method, comprising introducing into the mammal by disrupting the stratum corneum an effective dose of the target antigen or an epitope(s) thereof.

As detailed above, Dearman fails to teach introducing antigen into the mammal by disrupting the stratum corneum. Glenn teaches a method for vaccinating a mammal comprising the topical administration to intact skin (col. 2, line 53) of an antigen together with an activator of dendritic cells, wherein the activator is selected from the lipophilic molecules, trinitrochlorobenzene, dinitrofluorobenzene, pentadecylcatechol and lipid A. Glenn's topical introduction of antigen via permeation through intact skin avoids disrupting the stratum corneum. Thus, the combination fails to teach a vaccination method, comprising *inter alia* introducing into the mammal by disrupting the stratum corneum an effective dose of the target antigen or an

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epitope(s) thereof as recited in all of new Claims 60-85. Accordingly, Applicant respectfully asserts that Dearman in view of Glenn cannot render obvious any of new Claims 60-85.

Double patenting rejections

The Examiner maintained the rejection of Claims 1, 6, 8, 11, 13-19, 21-24, 27-31, 51-53, 55 and 58 under the judicially created doctrine of obviousness-type double patenting over claims 1-21 of US patent 6,210,672.

Applicant appreciates the Examiner's acknowledgement that a terminal disclaimer will be filed at the time allowable subject matter is indicated.

CONCLUSION

Applicant has addressed all of the Examiner's concerns as expressed in the outstanding Office Communications dated March 9, 2005 and August 23, 2005. If the Examiner finds any remaining impediment to the prompt allowance of the pending claims that could be clarified with a telephone conference, the Examiner is respectfully invited to call the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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